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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,744	05/04/2005	Willliam Brown	100886-1P US	4550

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EXAMINER	
BERNHARDT, EMILY B	
ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,744	BROWN ET AL.	
	Examiner	Art Unit	
	Emily Bernhardt	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 8-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 8-12* is/are rejected.

7)☒ Claim(s) *2-5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/12/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

.Claims 1, and 8-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
1. Nature of optional substiuents permitted at R1 and R2 is not clesrly defined in the specification. While a list of intended moieties are described on p.4-5 , the intended scope is not limited to said list. Note the wording "exemplary chemical groups....include". A similar issue was present in Ex parte Remark 15 USPQ 2d 1498 (at p.1500) in which it was decided that claim language that relied on open-ended language was "vague and uncertain" since it was not clear what else was intended to be covered.

Claims 1 and 8-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for subject matter embraced in dependent claims 2-5, does not reasonably provide enablement for entire scope claimed at R1/R2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

There is no reasonable basis for assuming that the myriad of compounds

embraced by the claims will all share the disclosed physiological properties since they are so structurally dissimilar as to being chemically non-equivalent and there is no basis in the prior art for assuming the same. From a reading of the specification the scope of " heterocyclyl" alone is huge encompassing just about any ring containing one or more of N,O and S both saturated and unsaturated and aromatic and both fused and unfused. Heteroaromatics can include N,O,P and S in any array and is also not limited to monocyclic rings. See specification on p.3-5 . Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art. Also note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a), August 2000 edition which includes such factors as:

1) Breadth of the claims- the claims cover compounds easily in the millions if not billions as pointed out above;

2) Level of unpredictability in the art- the invention is pharmaceutical in nature as it involves agonist activity at a particular opioid receptor (δ). It is well established that "the scope of enablement varies inversely with the

degree of unpredictability of the factors involved" and physiological activity is generally considered to be unpredictable. See In re Fisher 166 USPQ 18;

3) Direction or guidance- as stated above compounds actually made and tested are much closer to each other than to remaining scope ;

4) State of the prior art- The compounds are 1-benzyhydryl piperazines with benzyl or heteroaralkyl groups at other N terminus. The phenyl rings must each be further substituted by carbamoyl groups. While such compounds having the same backbone are known in the prior art as evidenced by the art cited by applicants, they do not particularly suggest the mandatory substitution required herein nor the scope of hetero rings permitted at R1;

5) Working examples- The test data presented provides no clear evaluation of how **representative** rings at R1/R2 might affect potency to a large or small degree.

In view of the above considerations, this rejection is being applied.

Claim 10 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most

nearly connected, to make and/or use the invention.

The notion that selectivity at the delta receptor is indicative for treating any and all gastrointestinal disorders is not remotely substantiated by the current state of the art. See for example, Synder, cited by applicants who makes no such assertions. Indeed, Nortey also cited by applicants teaches compounds as delta agonists ,which has been well documented in the literature for treating pain covered in claim 9. This given the level of skill in this art which is low coupled with the many compounds covered and uses embraced by "gastrointestinal" disorders (such as diseases of the GI tract, ulcerative colitis, pancreatitis, reflux disease, dysphagia and many, many other diseases) this rejection is being applied.

Claims 2-5 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicants' IDS filed 8/12/05 has been considered as well as the international search report. Note entry B20 is a duplicate of B5 so has been crossed out. The two WO references particularly pointed out by the EPO examiner are too diffuse for suggesting instant $C(=O)N(H)R^2$ group at 2^{nd} phenyl which appears to be the advance over the art. There are no such

species described much less with additional features claimed herein. WO'215 is directed to piperidin-4-ylidene derivatives.

The list of copending applications on p.1 of the IDS have been also considered. A signed copy is being forwarded to applicants.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is 571-272-0664.

If attempts to reach the examiner by telephone are unsuccessful, the acting supervisor for AU 1624, James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

E Bernhardt

Emily Bernhardt
Primary Examiner
Art Unit 1624